

## Guidance on Chlorthalidone

This guidance represents the current thinking of the Food and Drug Administration (FDA, or the Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Office of Generic Drugs.

**Active Ingredient:** Chlorthalidone

**Dosage Form; Route:** Tablet; oral

**Recommended Studies:** Two studies

1. Type of study: Fasting  
Design: Single-dose, two-way crossover in vivo  
Strength: 50 mg  
Subjects: Healthy males and nonpregnant females, general population.  
Additional Comments: You may also consider using a parallel study design due to chlorthalidone's long half-life. For long half-life drug products, an AUC truncated at 72 hours may be used in place of  $AUC_{0-t}$  or  $AUC_{0-\infty}$ .

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2. Type of study: Fed  
Design: Single-dose, two-way crossover in vivo  
Strength: 50 mg  
Subjects: Healthy males and nonpregnant females, general population.  
Additional Comments: See comments above.

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**Analytes to measure (in appropriate biological fluid):** Chlorthalidone in plasma

**Bioequivalence based on (90% CI):** Chlorthalidone

**Waiver request of in-vivo testing:** 15 mg and 25 mg based on (i) acceptable bioequivalence studies on the 50 mg strength (ii) proportional similarity of the formulations across all strengths, and (iii) acceptable in vitro dissolution testing of all strengths.

**Dissolution test method and sampling times:** The dissolution information for this drug product can be found on the FDA-Recommended Dissolution Methods website, available to the public at the following location: <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application (ANDA).